Claims

1. A MHC class II antigenic peptide comprising
(a) at least the amino acid sequence of the peptide binding motif selected from the group consisting of SEQ ID NOs. 49 to 57 and SEQ ID NOs. 103 to 122, or
(b) at least the amino acid sequence of the peptide binding motif selected from the group consisting of SEQ ID NOs. 49 to 57 and SEQ ID NOs. 103 to 122, with additional N-and C-terminal flanking sequences of a corresponding sequence selected from the group consisting of SEQ ID NOs. 1 to 39 and SEQ ID NOs. 58 to 102.

2. A MHC class II antigenic peptide comprising
(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 49, or
(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 49 with additional N-and C-terminal flanking sequences of a corresponding sequence selected from the group consisting of SEQ ID NOs. 1 to 3.

3. A MHC class II antigenic peptide comprising
(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 103, or
(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 103 with additional N-and C-terminal flanking sequences of the corresponding sequence of SEQ ID NOs. 58 and 59.

4. A MHC class II antigenic peptide comprising
(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 104, or
(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 104 with additional N-and C-terminal flanking sequences of the corresponding sequence of SEQ ID NO. 60.

5. A MHC class II antigenic peptide comprising
(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 105, or
(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 105 with additional N-and C-terminal flanking sequences of the corresponding sequence of SEQ ID NO. 61.

6. A MHC class II antigenic peptide comprising
(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO.

106, or

(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 106 with additional N-and C-terminal flanking sequences of the corresponding sequence of SEQ ID NO. 62.

7. A MHC class II antigenic peptide comprising

(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 107, or

(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 107 with additional N-and C-terminal flanking sequences of the corresponding sequence of SEQ ID NO. 63.

8. A MHC class II antigenic peptide comprising

(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 50, or

(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 50 with additional N-and C-terminal flanking sequences of the corresponding sequence of SEQ ID NO. 5.

9. A MHC class II antigenic peptide comprising

(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 108, or

(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 108 with additional N-and C-terminal flanking sequences of the corresponding sequence of SEQ ID NOs. 64 to 67.

10. A MHC class II antigenic peptide comprising

(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 109, or

(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 109 with additional N-and C-terminal flanking sequences of the corresponding sequence of SEQ ID NO. 68.

11. A MHC class II antigenic peptide comprising

(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 110, or

(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 110 with additional N-and C-terminal flanking sequences of the corresponding sequence of SEQ ID NOs. 69 and 70.

12. A MHC class II antigenic peptide comprising
(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 111, or
(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 111 with additional N-and C-terminal flanking sequences of the corresponding sequence of SEQ ID NO. 72.

13. A MHC class II antigenic peptide comprising
(a) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 112, or
(b) at least the amino acid sequence of the peptide binding motif of SEQ ID NO. 112 with additional N-and C-terminal flanking sequences of the corresponding sequence of SEQ ID NO. 73.

14. The MHC class II antigenic peptide according to any one of claims 1 to 13 linked to a MHC class II molecule.

15. An antibody reactive with a MHC class II antigenic peptide according to any one of claims 1 to 13.

16. A nucleic acid molecule encoding a peptide or polypeptide according to any one of claims 1 to 14.

17. A recombinant nucleic acid construct comprising the nucleic acid molecule according to claim 16 operably linked to an expression vector.

18. A host cell containing the nucleic acid construct according to claim 17.

19. A method for producing a MHC class II antigenic peptide according to any one of claims 1 to 13 comprising the steps of culturing the host cell of claim 18 under conditions allowing expression of said peptide and recovering the peptide from the cells or the culture medium.

20. A method for isolating and identifying MHC class II associated RA antigenic peptides in femtomolar amounts, which method comprises
(a) providing immature dendritic cells in a number comprising 0.1 to 5 µg MHC class II molecules;
(b) contacting the cells of (a) with serum or synovial fluid and inducing maturation of dendritic cells by adding TNFalpha;
(c) isolating class II MHC molecule-antigenic peptide complexes from the cells with methods comprising solubilization of the cells and sequestration of the complexes

of MHC class II molecules with antigenic peptides by immunoprecipitation or immunoaffinity chromatography;
(d) washing the sequestered complexes of MHC class II molecules with antigenic peptides with water in an ultrafiltration tube;
(e) eluting the associated antigenic peptides from the MHC class II molecules at 37°C with diluted trifluoro acetic acid, and
(f) separating, detecting and identifying the isolated peptides by liquid chromatography and mass spectrometry.

21. The method according to claim 20, wherein in step (f) of the method the liquid chromatography comprises a first linear elution step from the reversed-phase material with a volume sufficient to elute contaminants prior to the peptide elution step.

22. The method according to any one of claims 20 and 21, further comprising
(g) analyzing the identified peptides by methods comprising a database and a software developed to perform comparative data analysis across multiple datasets.

23. A pharmaceutical composition comprising a MHC class II antigenic peptide according to any one of claims 1 to 13, an antibody according to claim 15, or a polypeptide selected from the group consisting of SEQ ID NOs 40 to 48 and SEQ ID NOs. 123 to 141, and optionally a pharmaceutically acceptable carrier.

24. A diagnostic composition comprising the antibody according to claim 15.

25. The use of the MHC class II antigenic peptide according to claim 1, wherein the antigenic peptide is a marker for erosive and/or non-erosive RA.

26. The use of the MHC class II antigenic peptide according to any one of claims 2 to 7, wherein the antigenic peptide is a marker for non-erosive RA.

27. The use of the MHC class II antigenic peptide according to any one of claims 8 to 13, wherein the antigenic peptide is a marker for erosive RA.

28. The use of a polypeptide selected from the group consisting of SEQ ID NOs 40 to 48 and SEQ. ID NOs. 123 to 141 as a marker for RA, preferably for erosive and/or non-erosive RA.

29. The antigenic peptides, antibodies, nucleic acids, host cells, methods, compositions and uses substantially as herein before described especially with reference to the foregoing Examples.

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